TABLE 1

Effect of LA and sham treatments on the total lipid concentrations in livers and aortae of hypedipidaemic roosters

	UNTREATED	TREATED FOUR APHAERESIS APPLICATIONS	
	CONTROLS n = 15	SHAM n = 15	LA n = 15
LIVER[a]	3.65 ± 0.98	5.53 ± 1.50[b]	3.72 ± 1.00[b]
AORTA[a]	6.01 ± 0.97	8.11 ± 2.15[c]	6.13 ± 0.95[c]

[a]Total lipid concentrations expressed as g lipid per 100 g tissue, mean ± SD
[b][c]p values were <0.05 when sham treatments were compared with LA treatments.
There were no statistical differences between the values of corresponding tissues in the untreated control group and the LA treated group.
All animals were sacrificed two days after the final aphaeresis treatment.

Humans

Patients have the plasmapheresis procedure undertaken using known transvenous techniques and plasmapheresis systems.

Plasmapheresis is performed using vein-to-vein or arteriovenous fistula in the forearm of patients. Heparin is given at the beginning of the procedure as a 5,000 unit bolus, and then by continuous infusion at the rate of 700 units per hour over the course of the procedure. Access through the antecubital veins should provide plasma flow rates of 25 to 40 mls per minute.

Blood taken from a patient is immediately treated with ACD-A (anticoagulant) in a ratio of between 1:8 and 1:16 (ACD-A:blood). The plasma is separated from this solution using a conventional plasmapheresis machine.

Twenty five percent plasma is removed from the patient. This represents one percent of the ideal body weight.

Only the first volume of plasma collection is replaced with plasma replacement fluid to the patient.

The plasma is kept refrigerated up until twelve hours prior to reinfusion of delipidated plasma in exchange for another twenty five percent plasma collection (weekly or biweekly).

The plasma is delipidated and the delipidated plasma is tested to ensure all solvent has been removed before the clean delipidated plasma is exchanged for new untreated plasma.

In one embodiment of the present invention, the continuous flow system described in U.S. Pat. No. 4,895,558 (the entire content of which is included herein) is modified to a discontinuous system by removing the appropriate blood volume to be treated and subjecting that volume to delipidation at a site remote from the patient.

In another embodiment of the present invention, the continuous flow system described in International Patent Application No. PCT/AU94/00415 (the entire content of which is included herein) is modified to a discontinuous system by removing the appropriate blood volume to be a site remote from the patient before the plasma is dispersed into small droplets into the solvent by the dispersing means.

In either of the above embodiments, the extraction step can include, in accordance with the present invention, either multiple washing of the extracted phase and/or using an absorbent.

For example, the plasma is delipidated with a solvent mixture comprising 1-butanol and di-isopropyl ether. The delipidated fraction is then washed three (3) or four (4) times with diethyl ether. After the final wash, the diethyl ether is removed by centrifugation and vacuum extraction at 37° C. The sintered spheres containing Bio-Beads SM-2 are then mixed with the delipidated plasma to remove the final traces of 1-butanol.

Sub a'

Conclusions

DES administration to the roosters resulted in a significant amount of fat (lipid) accumulation in the livers and aortae.

Discontinuous LA treatments corresponding to approximately one plasma volume treated by four applications of 25% of plasma volume treated per time resulted in significant decreases in both hepatic and aortic lipids in hyperlipidaemic animals. Moreover, the LA treated hyperlipidaemic animals ended up with lipid values that were similar to control animals.

(i) These experiments show that excessive amounts of body fats in the form of adipose tissue (triglycerides) in the liver can be removed by LA; and

(ii) regression of atherosclerosis occurs in the aorta by LA treatments.

Similar results can be expected for human patients.

By adapting the prior art methods to discontinuous flow systems, the present invention can remove or at least significantly reduce any danger to patients and medical staff from the explosive nature of the solvents employed.

Further, by using the improved solvent extraction methods of the present invention, all of the potentially poisonous extraction solvents can be removed before the treated blood is returned to the patient.

Also, the improved solvent extraction method of the present invention is not limited to plasma delipidation but also it is applicable to the delipidation of serum, thus providing advantageous changes to the blood rheology of the originally impaired blood circulation of the patient.

The present invention thus provides for a rapid regression of coronary atherosclerosis in a patient.

Finally, as the present invention is a discontinuous system, it is not essential to return the delipidated blood fraction immediately to the patient. It is already known that plasma or serum can be collected and stored under sterile conditions in a refrigerator or freezer for extended periods and that it can be returned safely to the patient within twelve (12) hours of breaking the sterile seal. Therefore, if necessary, reintroduction of the delipidated fraction can occur several weeks after it was first removed from the patient. This option leads to particular advantages such as, economics of scale when several patients have to be treated simultaneously, the freeing of medical staff and equipment for other duties, and the reduction in stress for the patient whom no longer has to be hooked up to a delipidation apparatus for several continuous hours. Further, it enables a bank of plasma or serum to be maintained which is free of any infection which can be delipidated and exchanged for a patient's plasma or serum as required. Of course, autologous or non-autologous plasma or serum could be returned to the patient under these conditions.

The embodiments are described by way of illustrative examples only and various changes and modifications may be made thereto without departing from the inventive concept as defined in the following claims.

I claim:

1. A method for the removal of cholesterol, triglycerides and other lipids from animal plasma, serum, or other suitable blood fraction containing apolipoproteins, as a discontinuous flow system, said method comprising connecting a subject to a device for withdrawing blood, withdrawing blood containing blood cells from the subject, separating said fraction from the blood cells and mixing with a solvent mixture which extracts said lipids from the fraction but which does not extract said apolipoproteins from the fraction, after which the delipidated fraction is recombined

with the blood cells and returned to the subject, such that the solve it extraction step is carried out separately and remote from the subject while the subject is not still connected to the device for withdrawing blood from the subject, wherein the extraction solvent is removed from the delipidated fraction by mixing the delipidated fraction with an absorbent specific for the extraction solvent and wherein the absorbent does not remove said apolipoproteins from the delipilidated fraction being returned to the subject.

2. A method as defined in claim 1, wherein the extraction solvent is substantially removed from the delipidated fraction by washing with a second solvent.

3. A method as defined in claim 2, wherein the delipidated fraction is washed four times.

4. A method as defined in claim 2, wherein the second solvent is diethyl ether.

5. A method as defined in claim 1, wherein the absorbent is contained in the pores of sintered spheres.

6. A method as defined in claim 5, wherein the sintered spheres are about 2 mm to 5 mm in diameter and the pores of the spheres are less than 50 Å in diameter.

7. A method as defined in claim 1, wherein the absorbent is a macroporous polymeric bead for absorbing organic molecules from an aqueous solution.

8. A method as defined in any one of claim 1, wherein the absorbent is held in a chamber which is adapted to allow the delipidated fraction to pass through or over the absorbent at least twice.

9. A porous sintered sphere for use in a method as defined in claim 1, said sphere containing an absorbent in its pores.

10. A sintered sphere as defined in claim 9, wherein the absorbent is a macroporous polymeric bead for absorbing organic molecules from an aqueous solution.

11. A method of changing the blood rheology of an animal with impaired blood circulation whereby the plasma, serum or other suitable blood fraction of the animal has been treated by a method as defined in claim 1.

12. A method for rapid regression of coronary atherosclerosis in an animal whereby the plasma, serum or other suitable blood fraction from the animal is treated by a method as defined in claim 1.

13. A method of removing excessive adipose tissue from an animal whereby the plasma, serum or other suitable blood fraction from the animal is treated by a method as defined in claim 1.

14. A method of removing fat soluble toxins from an animal whereby the plasma, serum or other suitable blood fraction from the animal is treated by a method as defined in claim 1.

15. A method of changing the blood rheology of an animal whereby the plasma or serum of the animal is exchanged for non-autologous plasma or serum wherein said non-autologous plasma or serum has been treated by a method as defined in of claim 1.

16. A method of rapidly regressing coronary atherosclerosis in an animal whereby the plasma or serum of the animal is exchanged for non-autologous plasma or serum wherein said non-autologous plasma or serum has been treated by a method as defined in claim 1.

17. A method of removing excessive adipose tissue from an animal whereby the plasma or serum of the animal is exchanged for non-autologous plasma or serum wherein said non-autologous plasma or serum has been treated by a method as defined in claim 1.

18. A method of removing fat soluble toxins from an animal whereby the plasma or serum of the animal is exchanged for non-autologous plasma or serum wherein said non-autologous plasma or serum has been treated by a method as defined in claim 1.

19. A method for the removal of cholesterol, triglycerides and other lipids from animal plasma, serum, or other suitable blood fraction containing apolipoproteins, a discontinuous flow system, said method comprising connecting a subject to a device for withdrawing blood, withdrawing blood containing blood cells from the subject, separating said fraction from the blood cells and mixing with a solvent mixture which extracts said lipids from the fraction but which does not extract said apolipoproteins from the fraction, after which the delipidated fraction is is recombined with the blood cells and returned to the subject such that the solvent extraction step is carried out separately and remote from the subject while the subject is not still connected to the device for withdrawing blood from the subject, wherein the solvent extraction step comprises:

(a) mixing the solvent mixture containing the fraction with beads, said beads being of a density substantially mid-way between the density of the fraction and the density of the solvent mixture; and

(b) isolating the thus delipidated fraction-containing phase.

20. A method as defined in claim 19, wherein the beads contain entrapped air to obtain the density substantially midway between the density of the fraction and the density of the solvent mixture.

21. A method as defined in claim 20, wherein the density of the beads is about 0.9 g/ml.

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